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☐ 1. Document ID: US 20020142301 A1

L1: Entry 1 of 3 File: PGPB Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020142301
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020142301 A1

TITLE: Method and apparatus for simultaneous quantification of different radionuclides in a large number of regions on the surface of a biological microarray or similar test objects

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hovig, Eivind	Oslo		NO	
Skretting, Arne	Slependen		NO	
Nygard, Einar	Asker		NO	
Kvinnsland, Yngve	Rykkinn		NO	
Breistol, Knut	Oslo		NO	
Yoshioka, Koki	Oslo		NO	

US-CL-CURRENT: 435/6; 378/1, 702/20

ABSTRACT:

The present invention relates to a method and apparatus for simultaneous quantification of the amounts of one or more radioactive nuclides within arbitrary regions on a surface where these nuclides have been deposited, adsorbed or fixed. These radioactive nuclides serve as markers on compounds that typically have been incorporated into tissue sections or into larger biological molecules that by various mechanisms have been bound to chemical substances on this surface. The method is especially well suited for DNA microarray deductions through the use of nucleotides labelled with different beta-emitting radionuclides.

L1: Entry 1 of 3 File: PGPB Oct 3, 2002

DOCUMENT-IDENTIFIER: US 20020142301 A1
TITLE: Method and apparatus for simultaneous quantification of different radionuclides in a large number of regions on the surface of a biological microarray or similar test objects

Detail Description Paragraph (31):
[0057] After calibration of the instrument, and prior to the measurements of the DNA microarray, the spectra of .sup.33P and .sup.35S were measured separately as follows: Solutions of the radionuclides were deposited evenly on glass slides and allowed to dry. The multiple energy band images obtained with these slides had an energy bin size of 15 keV, and there were 20 bins starting at a lower threshold of 20 keV. The spectra were spectra were created using the same bin sizes and number of bins and assumed to be independent of the position on the detector, therefore the

entire images contributed to the spectra. For each pixel (or dot), the unknown contributions P and S from .sup.33P and .sup.35S respectively, were determined by the regression analysis and also by the Maximum Likelihood procedure. The resulting images P and S were displayed as one single image in the mode commonly used for presentation of images obtained with fluorophores. The phosphorus image (P) was sent to the red channel of the display, and the sulphur image was sent to the green channel. Equal amounts of red and green thus gave a yellow colour.

☐ 2. Document ID: US 20020107640 A1

L1: Entry 2 of 3 File: PGPB Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020107640
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020107640 A1

TITLE: Methods for determining the true signal of an analyte

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ideker, Trey E.	Cambridge	MA	US	
Thorsson, Vesteinn	Seattle	WA	US	
Siegel, Andrew F.	Seattle	WA	US	

US-CL-CURRENT: 702/19; 702/22, 702/25, 708/131

ABSTRACT:

The invention relates to a method of determining a true signal of an analyte, comprising (a) measuring an observed signal x for one or more analytes, and (b) determining a mean signal (.mu.) and a system parameter (.beta.) for said analyte that produce enhanced values for a probability likelihood of said observed signal, said observed signal being related to said mean signal by an additive error (.delta.) and a multiplicative error (.epsilon.), wherein said system parameter specifies properties of said additive error (.delta.) and said multiplicative error (.epsilon.).

L1: Entry 2 of 3 File: PGPB Aug 8, 2002

DOCUMENT-IDENTIFIER: US 20020107640 A1
TITLE: Methods for determining the true signal of an analyte

Cross Reference to Related Applications Paragraph (1):
[0001] This application is based on, and claims the benefit of, U.S. Provisional Application No. 60/248,259, filed Nov. 14, 2000, entitled Testing for Differentially-Expressed Genes by Maximum Likelihood Analysis of Microarray Data and claims benefit of, U.S. Provisional Application No. 60/266,388, filed Feb. 2, 2001, entitled Methods for Determining the True Signal of an Analyte, which are incorporated herein by reference.

Detail Description Paragraph (14):
[0024] For comparison of two signals, the maximum-likelihood approach provided by the invention has several advantages over currently accepted ratio-based significance tests. In the ratio-based method, the expression ratio for the two

signals to be compared is computed and compared to a control or reference ratio. For example, where the relative level of an analyte is to be compared under two different conditions, the ratio r.sub.i=x.sub.i/y.sub.i is computed for analyte i for the two conditions x and y, and compared to a reference ratio of known analyte signals. A ratio that differs from the reference ratio, for example, as r.sub.i>r.sub.c or r.sub.i<1/r.sub.c identifies the analyte levels under the two conditions as being meaningfully different. This ratio-based method has been widely used in fields that compare, for example, the differences in expression of RNA or protein under two different conditions. The method has been particularly applicable to large scale expression analysis such as those utilizing microarray formats. However, the ratio-based method for statistical analysis of signal data combines observed signals into a single ratio, which necessarily results in the loss of absolute signal information. Moreover, when repeated samples per analyte are available, common practice is to compute the ratio of averaged signals, again discarding useful information.

Detail Description Paragraph (73):
[0078] This example describes development of a maximum-likelihood test for the variability observed over repeated observations of intensities for genes represented on a DNA microarray.

Detail Description Paragraph (109):
[0110] Each gene was represented by two spots located on opposite sides of the array. A total of four (x,y) intensity pairs was obtained for each gene by performing replicate hybridizations to two of the above microarrays (N=6200, M=4), with x and y representing intensities in YPR and YPRG respectively. In the first hybridization, RNA from the YPR condition was labeled with Cy3 dye, while RNA from the YPRG condition was labeled with Cy5 dye; in the second hybridization the reverse labeling scheme was used. The .beta. and .mu. values were determined for these data using our maximum likelihood approach, and the .lambda..sub.1 statistic was computed for each gene. Values for .beta. were as follows: 0.367, 0.391, 0.862, 89.6, 339.0, 0.319.

☐ 3. Document ID: US 6607886 B2

L1: Entry 3 of 3 File: USPT Aug 19, 2003

US-PAT-NO: 6607886
DOCUMENT-IDENTIFIER: US 6607886 B2

TITLE: Method and apparatus for simultaneous quantification of different radionuclides in a large number of regions on the surface of a biological microarray or similar test objects

DATE-ISSUED: August 19, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hovig; Eivind	Oslo			NO
Skretting; Arne	Slependen			NO
Nygard; Einar	Asker			NO
Kvinnsland; Yngve	Rykkinn			NO
Breistol; Knut	Oslo			NO
Yoshioka; Koki	Oslo			NO

US-CL-CURRENT: 435/6; 435/196, 435/320.1, 435/7.6, 536/23.1, 536/23.2, 536/24.1

ABSTRACT:

The present invention relates to a method and apparatus for simultaneous quantification of the amounts of one or more radioactive nuclides within arbitrary regions on a surface where these nuclides have been deposited, adsorbed or fixed. These radioactive nuclides serve as markers on compounds that typically have been incorporated into tissue sections or into larger biological molecules that by various mechanisms have been bound to chemical substances on this surface. The method is especially well suited for DNA microarray deductions through the use of nucleotides labelled with different beta-emitting radionuclides.

12 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

L1: Entry 3 of 3 File: USPT Aug 19, 2003

DOCUMENT-IDENTIFIER: US 6607886 B2
TITLE: Method and apparatus for simultaneous quantification of different radionuclides in a large number of regions on the surface of a biological microarray or similar test objects

Detailed Description Text (28):
After calibration of the instrument, and prior to the measurements of the DNA microarray, the spectra of .sup.33 P and .sup.35 S were measured separately as follows: Solutions of the radionuclides were deposited evenly on glass slides and allowed to dry. The multiple energy band images obtained with these slides had an energy bin size of 15 keV, and there were 20 bins starting at a lower threshold of 20 keV. The spectra were spectra were created using the same bin sizes and number of bins and assumed to be independent of the position on the detector, therefore the entire images contributed to the spectra. For each pixel (or dot), the unknown contributions P and S from .sup.33 P and .sup.35 S respectively, were determined by the regression analysis and also by the Maximum Likelihood procedure. The resulting images P and S were displayed as one single image in the mode commonly used for presentation of images obtained with fluorophores. The phosphorus image (P) was sent to the red channel of the display, and the sulphur image was sent to the green channel. Equal amounts of red and green thus gave a yellow colour.

Term	Documents
MICROARRAY	6194
MICROARRAYS	5926
SIGNAL	3187003
SIGNALS	1610311
TO	39647
NOISE	641173
NOISES	55702
NOIZE	234
NOIZES	11
MAXIMUM	1234374
MAX	210598
(MICROARRAY SAME ((SIGNAL TO NOISE) OR (MAXIMUM LIKELIHOOD))).USPT,PGPB,JPAB,EPAB,DWPI.	3

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NEWS 4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
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NEWS 6	Jul 21	Polymer class term count added to REGISTRY
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L1 51 MICROARRAY AND ((SIGNAL TO NOISE) OR (MAXIMUM LIKELIHOOD))

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L2 ANSWER 1 OF 37 MEDLINE on STN DUPLICATE 1
AN 2003274876 IN-PROCESS
DN 22686122 PubMed ID: 12801865
TI Statistical adjustment of signal censoring in gene expression experiments.
AU Wit Ernst; McClure John
CS Department of Statistics, University of Glasgow, Glasgow G12 8QW, UK..
ernst@stats.gla.ac.uk
SO BIOINFORMATICS, (2003 Jun 12) 19 (9) 1055-60.
Journal code: 9808944. ISSN: 1367-4803.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030613
Last Updated on STN: 20030702
AB MOTIVATION: Numerical output of spotted **microarrays** displays censoring of pixel intensities at some software dependent threshold. This reduces the quality of gene expression data, because it seriously violates the linearity of expression with respect to signal intensity. Statistical methods based on typically available spot summaries together with some parametric assumptions can suggest ways to correct for this defect. RESULTS: A **maximum likelihood** approach is suggested together with a sensible approximation to the joint density of the mean, median and variance-which are typically available to the biological end-user. The method 'corrects' the gene expression values for pixel censoring. A by-product of our approach is a comparison between several two-parameter models for pixel intensity values. It suggests that pixels separated by one or two other pixels can be considered independent draws from a Lognormal or a Gamma distribution. AVAILABILITY: The R/S-Plus code is available at http://www.stats.gla.ac.uk/ **microarray** /software.

L2 ANSWER 2 OF 37 MEDLINE on STN
AN 2003415080 IN-PROCESS
DN 22835105 PubMed ID: 12809552
TI Synergistic effects of epoxy- and amine-silanes on **microarray** DNA immobilization and hybridization.
AU Chiu Sung-Kay; Hsu Mandy; Ku Wei-Chi; Tu Ching-Yu; Tseng Yu-Tien; Lau Wai-Kwan; Yan Rong-Yih; Ma Jing-Tyan; Tzeng Chi-Meng
CS Department of Research and Development, U-Vision Biotech Inc., 3F No.132 Lane 235 Pao-Chiao Rd, Hsin-Tien City 231, Taipei, Taiwan.
SO BIOCHEMICAL JOURNAL, (2003 Sep 15) 374 (Pt 3) 625-32.
Journal code: 2984726R. ISSN: 1470-8728.
CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030905
Last Updated on STN: 20030910
AB Most **microarray** slides are manufactured or coated with a layer of poly(L-lysine) or with silanes with different chemical functional groups, for the attachment of nucleic acids on to their surfaces. The efficiency with which nucleic acids bind to these surfaces is not high, because they can be washed away, especially in the case of spotting oligonucleotides. In view of this, we have developed a method to increase the binding capacity and efficiency of hybridization of DNA on to derivatized glass surfaces. This makes use of the synergistic effect of two binding interactions between the nucleic acids and the coating chemicals on the surface of the glass slides. The enhanced binding allows the nucleic acids to be bound tightly and to survive stringency washes. When immobilized, DNA exhibits a higher propensity for hybridization on the surface than on slides with only one binding chemical. By varying the silane concentrations, we have shown that maximal DNA oligonucleotide binding on glass surfaces occurs when the percentage composition of both of the surface-coating chemicals falls to 0.2%, which is different from that on binding PCR products. This new mixture-combination approach for nucleic-acid binding allows signals from immobilization and hybridization to have higher **signal**-to-**noise** ratios than for other silane-coated methods.

L2 ANSWER 3 OF 37 MEDLINE on STN DUPLICATE 2
AN 2003268584 IN-PROCESS
DN 22592360 PubMed ID: 12706560
TI High-density, microsphere-based fiber optic DNA **microarrays**.
AU Epstein Jason R; Leung Amy P K; Lee Kyong Hoon; Walt David R
CS The Max Tishler Laboratory for Organic Chemistry, Tufts University, Medford, MA 02155, USA.
SO BIOSENSORS AND BIOELECTRONICS, (2003 May) 18 (5-6) 541-6.
Journal code: 9001289. ISSN: 0956-5663.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030611
Last Updated on STN: 20030611
AB A high-density fiber optic DNA **microarray** has been developed consisting of oligonucleotide-functionalized, 3.1-microm-diameter microspheres randomly distributed on the etched face of an imaging fiber bundle. The fiber bundles are comprised of 6000-50000 fused optical fibers and each fiber terminates with an etched well. The microwell array is capable of housing complementary-sized microspheres, each containing thousands of copies of a unique oligonucleotide probe sequence. The array fabrication process results in random microsphere placement. Determining the position of microspheres in the random array requires an optical encoding scheme. This array platform provides many advantages over other array formats. The microsphere-stock suspension concentration added to the etched fiber can be controlled to provide inherent sensor redundancy. Examining identical microspheres has a beneficial effect on the **signal**-to-**noise** ratio. As other sequences of interest are discovered, new microsphere sensing elements can be added to existing microsphere pools and new arrays can be fabricated incorporating the new sequences without altering the existing detection capabilities. These **microarrays** contain the smallest feature sizes (3 microm) of any DNA array, allowing interrogation of extremely small sample volumes. Reducing the feature size results in higher local target molecule concentrations, creating rapid and highly sensitive assays. The microsphere array platform is also flexible in its applications; research has included DNA-protein interaction profiles, microbial strain

differentiation, and non-labeled target interrogation with molecular beacons. Fiber optic microsphere-based DNA **microarrays** have a simple fabrication protocol enabling their expansion into other applications, such as single cell-based assays.

L2 ANSWER 4 OF 37 MEDLINE on STN
AN 2003398186 IN-PROCESS
DN 22816857 PubMed ID: 12938086
TI Genotyping African haplotypes in ATM using a co-spotted single-base extension assay.
AU Jain Maneesh; Thorstenson Yvonne R; Faulkner David M; Pourmand Nader; Jones Ted; Au Melinda; Oefner Peter J; White Kevin P; Davis Ronald W
CS Stanford Genome Technology Center, Palo Alto, California 94304, USA.
NC HG00205 (NHGRI)
SO HUMAN MUTATION, (2003 Sep) 22 (3) 214-21.
Journal code: 9215429. ISSN: 1098-1004.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
OS GENBANK-U82828; OMIM-607585
ED Entered STN: 20030826
Last Updated on STN: 20030916
AB Human genetic analysis, including population genetic studies, increasingly calls for cost-effective, high-throughput methods for the rapid screening of single nucleotide polymorphisms (SNPs) across many individuals. The modified single-base extension assay described here (arrayed SBE) is a highly accurate and robust method for SNP genotyping that can deliver genotypes at 3.5 cents each, following PCR. Specifically, amino-modified probe/target pairs were prehybridized, then co-spotted in a **microarray** format prior to enzymatic addition of allele-specific nucleotides. Probe/target identity was determined solely by its physical location on the array rather than by hybridization to a complementary target, resulting in a call rate of 99-100%. These innovations result in an inexpensive, accurate assay with exceptional **signal**-to-**noise** ratios, depending on the glass surface employed. Comparison of glass slides from three different manufacturers indicated that aldehyde-based Zyomyx slides provided superior performance for this assay. Arrayed SBE was applied to study the geographic distribution of three African-specific haplotypes in the human ATM gene. Four selectively neutral markers, which define the haplotypes H5, H6, and H7, were screened in a total of 415 individuals. Region-specific haplotype frequencies were consistent with patterns of human migration across and outside of Africa, suggesting a possible haplotype origin in East Africa. Arrayed SBE was a robust tool for this analysis that could be applied to any situation requiring the genotyping of a few SNPs in many individuals.

L2 ANSWER 5 OF 37 MEDLINE on STN
AN 2003436762 IN-PROCESS
DN 22858333 PubMed ID: 13678150
TI Enhancing results of **microarray** hybridizations through microagitation.
AU Toegl Andreas; Kirchner Roland; Gauer Christoph; Wixforth Achim
CS Advalytix AG, Brunnthal, Germany.. toegl@advalytix.de
SO J Biomol Tech, (2003 Sep) 14 (3) 197-204.
Journal code: 100888641. ISSN: 1524-0215.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030919
Last Updated on STN: 20030919
AB Protein and DNA **microarrays** have become a standard tool in

proteomics/genomics research. In order to guarantee fast and reproducible hybridization results, the diffusion limit must be overcome. Surface acoustic wave (SAW) micro-agitation chips efficiently agitate the smallest sample volumes (down to 10 microL and below) without introducing any dead volume. The advantages are reduced reaction time, increased **signal**-to-**noise** ratio, improved homogeneity across the **microarray**, and better slide-to-slide reproducibility. The SAW micromixer chips are the heart of the Advalytix Array-Booster, which is compatible with all **microarrays** based on the microscope slide format.

L2 ANSWER 6 OF 37 MEDLINE on STN
AN 2003406710 IN-PROCESS
DN 22826246 PubMed ID: 12945746
TI Development of protein **microarray** technology to monitor biomarkers of rheumatoid arthritis disease.
AU Urbanowska T; Mangialaio S; Hartmann C; Legay F
CS Marker and Assay Development, Novartis Pharma, Basel, Switzerland.. teresa.urbanowska@pharma.novartis.com
SO CELL BIOLOGY AND TOXICOLOGY, (2003 Jun) 19 (3) 189-202. Journal code: 8506639. ISSN: 0742-2091.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030830
Last Updated on STN: 20030830
AB Most biological processes are mediated by complex networks of molecular interactions involving proteins. The analysis of protein expression in biological samples is especially important in the identification and monitoring of biomarkers for disease progression and therapeutic endpoints. In this paper, the development of a protein **microarray** format for multiplexed quantitative analysis of several potential markers for rheumatoid arthritis (RA) is described. Development of a high-performance protein **microarray** system depends on several key parameters such as surface chemistry, capture agents, immobilization technology, and methods used for signal detection and quantification. Several technical possibilities were investigated and compared: poly-L-lysine versus self-assembled monolayer of octadecyl phosphoric acid ester for surface chemistries; noncontact piezoelectric versus contact printing technology for antibody deposition; CCD camera capture versus fluorescent scanning for image detection; and the concentration of coating antibody. On the basis of reproducibility, **signal**-to-**noise** ratio, and sensitivity we have selected self-assembled monolayer, noncontact piezoelectric printer, and high-read-out fluorescence scanning for our **microarray** format. This format was used to perform multiplexed quantitative analysis of several potential markers of disease progression of rheumatoid arthritis: IL-1beta, IL-6, IL-8, MCP-1, and SAA. Some assays, such as MCP-1, provided a working range that covered physiologically relevant concentrations. Other assays, such as IL-6 and SAA, lacked sensitivity or were too sensitive for measuring biological concentrations, respectively. The results described demonstrate the applicability of protein **microarrays** to monitor RA markers; however, sandwich assay methodologies need to be further optimized to measure the appropriate biological ranges of these markers on one chip.

L2 ANSWER 7 OF 37 MEDLINE on STN
AN 2003071299 IN-PROCESS
DN 22469241 PubMed ID: 12581958
TI Two restriction fluorescence labeling methods for enhancing the **signal**-to-**noise** ratio of cDNA **microarray** hybridization.
AU Shi Rong; Ma Wen-Li; Song Yan-Bin; Li Ling; Liu Cui-Hua; Zheng Wen-Ling

CS Institute of Molecular Biology, First Military Medical University, Guangzhou 510515, China.
SO Di Yi Jun Yi Da Xue Xue Bao, (2003 Feb) 23 (2) 124-6. Journal code: 9426110. ISSN: 1000-2588.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030214
Last Updated on STN: 20030214
AB OBJECTIVE: To study the **signal**-to-**noise** ratio (SNR) of two restricted fluorescence labeling methods for examining gene expression profile by **microarray** hybridization. METHOD: Samples of Saccharomyces cerevisiae mRNA was labeled by traditional reverse transcription method and 2 restriction fluorescent labeling methods using respectively Cy-universal primer and extension incorporated Cy-dNTP. The labeled samples were examined by the **microarray**, followed by washing and scanning under the same conditions. RESULTS: The two restriction labeling methods showed superior results with lowered background and enhanced SNR and sensitivity, and Cy-universal primer labeling presented the best results. CONCLUSION: SNR can be enhanced by the restriction labeling methods, which improve the applicability of **microarray** technology.

L2 ANSWER 8 OF 37 MEDLINE on STN
AN 2003309569 IN-PROCESS
DN 22721687 PubMed ID: 12837263
TI Array rank order regression analysis for the detection of gene copy-number changes in human cancer.
AU Cheng Chun; Kimmel Robert; Neiman Paul; Zhao Lue Ping
CS Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue North, Seattle, WA 98109, USA.
NC R01-9M58897-03 (NCI)
R01-CA20068 (NHGRI)
R01-HG02283-02
SO GENOMICS, (2003 Aug) 82 (2) 122-9. Journal code: 8800135. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030703
Last Updated on STN: 20030724
AB cDNA **microarray** technology has been applied to the detection of DNA copy-number changes in malignant tumors. Test and control genomic DNA samples are differentially labeled and cohybridized to a spotted cDNA **microarray**. The ratio of test to control fluorescence intensities for each spot reflects relative gene copy number. The low **signal** -to-**noise** ratios of this assay and the variable levels of gene amplification and deletion among tumors hamper the detection of deviations from the diploid complement. We describe a regression-based statistical method to test for altered copy number on each gene and apply the technique to copy-number profiles in 10 thyroid tumors. We show that a novel transformation of fluorescence ratios into array rank order efficiently normalizes the heterogeneity among copy-number profiles and improves the reproducibility of the results. Array rank order regression analysis enhances the detection of consistent changes in gene copy number in solid tumors by cDNA **microarray**-based comparative genome hybridization.

L2 ANSWER 9 OF 37 MEDLINE on STN DUPLICATE 3
AN 2003040593 MEDLINE
DN 22436305 PubMed ID: 12548634
TI Antibody **microarray** profiling of human prostate cancer sera:

antibody screening and identification of potential biomarkers.
AU Miller Jeremy C; Zhou Heping; Kwekel Joshua; Cavallo Robert; Burke Jocelyn; Butler E Brian; Teh Bin S; Haab Brian B
CS The Van Andel Research Institute, Grand Rapids, MI 49503, USA.
SO Proteomics, (2003 Jan) 3 (1) 56-63.
Journal code: 101092707. ISSN: 1615-9853.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20030128
Last Updated on STN: 20030801
Entered Medline: 20030731
AB We developed a practical strategy for serum protein profiling using antibody **microarrays** and applied the method to the identification of potential biomarkers in prostate cancer serum. Protein abundances from 33 prostate cancer and 20 control serum samples were compared to abundances from a common reference pool using a two-color fluorescence assay. Robotically spotted **microarrays** containing 184 unique antibodies were prepared on two different substrates: polyacrylamide based hydrogels on glass and poly-1-lysine coated glass with a photoreactive cross-linking layer. The hydrogel substrate yielded an average six-fold higher **signal**-to-**noise** ratio than the other substrate, and detection of protein binding was possible from a greater number of antibodies using the hydrogels. A statistical filter based on the correlation of data from "reverse-labeled" experiment sets accurately predicted the agreement between the **microarray** measurements and enzyme-linked immunosorbent assay measurements, showing that this parameter can serve to screen for antibodies that are functional on **microarrays**. Having defined a set of reliable **microarray** measurements, we identified five proteins (von Willebrand Factor, immunoglobulinM, Alpha1-antichymotrypsin, Villin and immunoglobulinG) that had significantly different levels between the prostate cancer samples and the controls. These developments enable the immediate use of high-density antibody and protein **microarrays** in biomarker discovery studies.

L2 ANSWER 10 OF 37 MEDLINE on STN DUPLICATE 4
AN 2003028723 MEDLINE
DN 22423704 PubMed ID: 12536376
TI Analysis of several fluorescent detector molecules for protein **microarray** use.
AU Wiese Rick
CS Genometrix Inc, 2700 Research Forest Drive, The Woodlands, TX 77381, USA..
rick.wise@perbio.com
SO LUMINESCENCE, (2003 Jan-Feb) 18 (1) 25-30.
Journal code: 100889025. ISSN: 1522-7235.
CY England: United Kingdom
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200309
ED Entered STN: 20030122
Last Updated on STN: 20030918
Entered Medline: 20030917
AB The utility of several streptavidin-linked fluorescent detector molecules was evaluated on two protein **microarray** platforms. Tested detector molecules included: Alexa Fluor 546; R-phycoerythrin (RPE), orange fluospheres; Cy3-containing liposomes (Large Unilamellar Vesicles, LUV) labelled with Cy3; and an RPE-antibody complex. The two array architectures tested consisted of an array of murine Fc-biotin and an array of murine IgG (the murine IgG array was probed with a biotinylated

rabbit anti-murine IgG). These platforms allowed for the direct comparison of detector utility by detector recognition of array-bound biotin. All of the fluorescent detectors examined demonstrated utility on each of the array platforms. For the Fc-biotin array, detector signal intensity (background adjusted) was as follows: RPE-antibody complex > fluospheres > RPE > liposomes > Alexa 546: for the IgG array: RPE/antibody complex > RPE > fluospheres > Alexa546 > liposomes. The RPE-antibody complex fluoresced 67% and 150% more intensely than the next closest detector molecule for the Fc-biotin and the murine IgG arrays, respectively. A marked increase in background fluorescence (as compared to RPE alone) did not accompany the increase in signal intensity gained through RPE-antibody complex use (a true increase in **signal**: **noise** ratio). These results suggest that the RPE-antibody complex is superior to other molecules for fluorescent detection of analytes on protein **microarrays**.

=> d 11-20 bib ab

L2 ANSWER 11 OF 37 MEDLINE on STN
AN 2003317445 MEDLINE
DN 22730773 PubMed ID: 12803655
TI The construction and use of bacterial DNA **microarrays** based on an optimized two-stage PCR strategy.
AU Postier Bradley L; Wang Hong-Liang; Singh Abhay; Impson Lori; Andrews Heather L; Klahn Jessica; Li Hong; Risinger George; Pesta David; Deyholos Michael; Galbraith David W; Sherman Louis A; Burnap Robert L
CS Department of Microbiology & Molecular Genetics, Oklahoma State University, Stillwater, OK 74078 USA.. postier@biochem.okstate.edu
SO BMC Genomics, (2003 Jun 12) 4 (1) 23.
Journal code: 100965258. ISSN: 1471-2164.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20030709
Last Updated on STN: 20030729
Entered Medline: 20030728
AB BACKGROUND: DNA **microarrays** are a powerful tool with important applications such as global gene expression profiling. Construction of bacterial DNA **microarrays** from genomic sequence data using a two-stage PCR amplification approach for the production of arrayed DNA is attractive because it allows, in principal, the continued re-amplification of DNA fragments and facilitates further utilization of the DNA fragments for additional uses (e.g. over-expression of protein). We describe the successful construction and use of DNA **microarrays** by the two-stage amplification approach and discuss the technical challenges that were met and resolved during the project. RESULTS: Chimeric primers that contained both gene-specific and shared, universal sequence allowed the two-stage amplification of the 3,168 genes identified on the genome of Synechocystis sp. PCC6803, an important prokaryotic model organism for the study of oxygenic photosynthesis. The gene-specific component of the primer was of variable length to maintain uniform annealing temperatures during the 1st round of PCR synthesis, and situated to preserve full-length ORFs. Genes were truncated at 2 kb for efficient amplification, so that about 92% of the PCR fragments were full-length genes. The two-stage amplification had the additional advantage of normalizing the yield of PCR products and this improved the uniformity of DNA features robotically deposited onto the **microarray** surface. We also describe the techniques utilized to optimize hybridization conditions and **signal**-to-**noise** ratio of the transcription profile. The inter-lab transportability was demonstrated by

the virtual error-free amplification of the entire genome complement of 3,168 genes using the universal primers in partner labs. The printed slides have been successfully used to identify differentially expressed genes in response to a number of environmental conditions, including salt stress. CONCLUSIONS: The technique detailed here minimizes the cost and effort to replicate a PCR-generated DNA gene fragment library and facilitates several downstream processes (e.g. directional cloning of fragments and gene expression as affinity-tagged fusion proteins) beyond the primary objective of producing DNA **microarrays** for global gene expression profiling.

L2 ANSWER 12 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:270567 BIOSIS
DN PREV200300270567
TI Antibody **microarray** analysis of blood serum from cancer patients.
AU Haab, Brian B. (1); Zhou, Heping; Schotanus, Mark; Kaledas, Kerri; Diephouse, Daniel; Miller, Jeremy; Kwekel, Joshua; Burke, Jocelyn; Cavallo, Robert; Butler, E. Brian; Teh, Bin S.; Dillon, Deborah; Costa, Jose; Lizardi, Paul
CS (1) Van Andel Research Institute, 333 Bostwick, Grand Rapids, MI, 49503, USA: brian.haab@vai.org, heping.zhou@vai.org, mark.schotanus@vai.org, kerri.kaledas@vai.org, dan.diephouse@vai.org, jeremy.miller@vai.org, josh.kwekel@vai.org, brian.haab@cmgm.stanford.edu, rcavallo@packardbioscience.com, bhaab@zinc.cchem.berkeley.edu, bteh@bcm.tmc.edu, deborah.dillon@yale.edu, mailto:jose.costa@yale.edu, paul.lizardi@yale.edu USA
SO FASEB Journal, (March 2003, 2003) Vol. 17, No. 4-5, pp. Abstract No. 839.4. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome San Diego, CA, USA April 11-15, 2003 FASEB
. ISSN: 0892-6638.
DT Conference
LA English
AB Antibody **microarray** profiling of sera and other bodily fluids should offer new opportunities for biomarker discovery and insights into disease biology. We have used robotically spotted **microarrays** of antibodies and proteins to measure the relative abundances of multiple proteins in serum samples from prostate cancer and pancreatic cancer patients and controls. Serum proteins that had been coupled to either a fluorescent tag (e.g. Cy3) or a hapten (e.g. biotin) were incubated on the **microarrays**, and specific proteins bound to the immobilized molecules on the **microarrays** through specific interactions. After washing away unbound proteins, bound proteins were detected using the fluorescent tag or amplified signal (using rolling circle amplification) from the hapten-labeled proteins. An automated analysis process filters data by **signal**-to-**noise** ratio, averages replicate measurements, normalizes data, and filters data sets based on reproducibility. Comparisons of the **microarray** data with independently measured protein concentrations (by ELISA) validated the accuracy of the **microarray** measurements. Five serum proteins statistically distinguished a set of prostate cancer serum samples from the controls, and several serum proteins significantly varied between the pancreatic cancer patients and controls. Implications for the use of this technology in marker research and in the study of proteins in bodily fluids will be discussed.

L2 ANSWER 13 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:353868 BIOSIS
DN PREV200300353868
TI The construction and use of bacterial DNA **microarrays** based on an optimized two-stage PCR strategy.
AU Postier, Bradley L.; Wang, Hong-Liang; Singh, Abhay; Impson, Lori; Andrews, Heather L.; Klahn, Jessica; Li, Hong; Risinger, George; Pesta,

David; Deyholos, Michael; Galbraith, David W.; Sherman, Louis A.; Burnap, Robert L. (1)

CS (1) Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK, 74078, USA: postier@biochem.okstate.edu, hlwang31@hotmail.com, singh1@purdue.edu, impson@biochem.okstate.edu, heatherandrews7@hotmail.com, jessibear77@hotmail.com, hli@bilbo.bio.purdue.edu, risingg78@hotmail.com, davidpesta@hotmail.com, deyholos@ualberta.ca, galbraith@arizona.edu, lsherman@bilbo.bio.purdue.edu , Burnap@biochem.okstate.edu USA

SO BMC Genomics, (June 12 2003) Vol. 4, No. 23 Cited June 27, 2003, pp. No Pagination. http://www.biomedcentral.com/1471-2164. online. ISSN: 1471-2164.

DT Article

LA English

AB Background: DNA **microarrays** are a powerful tool with important applications such as global gene expression profiling. Construction of bacterial DNA **microarrays** from genomic sequence data using a two-stage PCR amplification approach for the production of arrayed DNA is attractive because it allows, in principal, the continued re-amplification of DNA fragments and facilitates further utilization of the DNA fragments for additional uses (e.g. over-expression of protein). We describe the successful construction and use of DNA **microarrays** by the two-stage amplification approach and discuss the technical challenges that were met and resolved during the project. Results: Chimeric primers that contained both gene-specific and shared, universal sequence allowed the two-stage amplification of the 3,168 genes identified on the genome of Synechocystis sp. PCC6803, an important prokaryotic model organism for the study of oxygenic photosynthesis. The gene-specific component of the primer was of variable length to maintain uniform annealing temperatures during the 1st round of PCR synthesis, and situated to preserve full-length ORFs. Genes were truncated at 2 kb for efficient amplification, so that about 92% of the PCR fragments were full-length genes. The two-stage amplification had the additional advantage of normalizing the yield of PCR products and this improved the uniformity of DNA features robotically deposited onto the **microarray** surface. We also describe the techniques utilized to optimize hybridization conditions and **signal**-to-**noise** ratio of the transcription profile. The inter-lab transportability was demonstrated by the virtual error-free amplification of the entire genome complement of 3,168 genes using the universal primers in partner labs. The printed slides have been successfully used to identify differentially expressed genes in response to a number of environmental conditions, including salt stress. Conclusions: The technique detailed here minimizes the cost and effort to replicate a PCR-generated DNA gene fragment library and facilitates several downstream processes (e.g. directional cloning of fragments and gene expression as affinity-tagged fusion proteins) beyond the primary objective of producing DNA **microarrays** for global gene expression profiling.

L2 ANSWER 14 OF 37 MEDLINE on STN

AN 2002313575 MEDLINE

DN 22001660 PubMed ID: 12005798

TI DNA hybridization to mismatched templates: a chip study.

AU Naef Felix; Lim Daniel A; Patil Nila; Magnasco Marcelo

CS Center for Studies in Physics and Biology, Rockefeller University, 1230 York Avenue, New York, New York 10021, USA.

SO Phys Rev E Stat Nonlin Soft Matter Phys, (2002 Apr) 65 (4 Pt 1) 040902. Journal code: 101136452. ISSN: 1539-3755.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200211

ED Entered STN: 20020612

Last Updated on STN: 20030105
Entered Medline: 20021108

AB High-density oligonucleotide arrays are among the most rapidly expanding technologies in biology today. In the GeneChip system, the reconstruction of the sample mRNA concentrations depends upon the differential signal generated by hybridizing the RNA to two nearly identical templates: a perfect match probe (PM) containing the exact biological sequence; and a single mismatch (MM) differing from the PM by a single base substitution. It has been observed that a large fraction of MMs repetitively bind targets better than the PMs, against the obvious expectation of sequence specificity. We examine this problem via statistical analysis of a large set of **microarray** experiments. We classify the probes according to their **signal** to **noise** (S/N) ratio, defined as the eccentricity of a (PM,MM) pair's "trajectory" across many experiments. Of those probes having large S/N (>3) only a fraction behave consistently with the commonly assumed hybridization model. Our results imply that the physics of DNA hybridization in **microarrays** is more complex than expected, and suggest estimators for the target RNA concentration.

L2 ANSWER 15 OF 37 MEDLINE on STN
AN 2002246634 MEDLINE
DN 21975967 PubMed ID: 11985315
TI High-density fiber-optic genosensor microsphere array capable of zeptomole detection limits.
AU Epstein Jason R; Lee Myoyong; Walt David R
CS The Max Tishler Laboratory for Organic Chemistry, Department of Chemistry, Tufts University, Medford, Massachusetts 02155, USA.
NC GM48142 (NIGMS)
SO ANALYTICAL CHEMISTRY, (2002 Apr 15) 74 (8) 1836-40.
Journal code: 0370536. ISSN: 0003-2700.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020503
Last Updated on STN: 20020528
Entered Medline: 20020523

AB The detection limit of a fiber-optic microsensor array was investigated for simultaneous detection of multiple DNA sequences. A random array composed of oligonucleotide-functionalized 3.1-microm-diameter microspheres on the distal face of a 500-microm etched imaging fiber was monitored for binding to fluorescently labeled complementary DNA sequences. Inherent sensor redundancy in the **microarray** allows the use of multiple microspheres to increase the **signal**-to-**noise** ratio, further enhancing the detection capabilities. Specific hybridization was observed for each of three sequences in an array yielding a detection limit of 10(-21) mol (approximately 600 DNA molecules).

L2 ANSWER 16 OF 37 MEDLINE on STN DUPLICATE 5
AN 2002727931 MEDLINE
DN 22378296 PubMed ID: 12490448
TI Statistical analysis of high-density oligonucleotide arrays: a multiplicative noise model.
AU Sasik R; Calvo E; Corbeil J
CS School of Medicine, University of California San Diego, La Jolla, CA 92093-0679, USA.. sasik@corgon.ucsd.edu
NC AI36214 (NIAID)
AI46237 (NIAID)
AI47703 (NIAID)
SO BIOINFORMATICS, (2002 Dec) 18 (12) 1633-40.
Journal code: 9808944. ISSN: 1367-4803.
CY England: United Kingdom

DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(VALIDATION STUDIES)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20021220
Last Updated on STN: 20030703
Entered Medline: 20030702
AB MOTIVATION: High-density oligonucleotide arrays (GeneChip, Affymetrix, Santa Clara, CA) have become a standard research tool in many areas of biomedical research. They quantitatively monitor the expression of thousands of genes simultaneously by measuring fluorescence from gene-specific targets or probes. The relationship between signal intensities and transcript abundance as well as normalization issues have been the focus of much recent attention (Hill et al., 2001; Chudin et al., 2002; Naef et al., 2002a). It is desirable that a researcher has the best possible analytical tools to make the most of the information that this powerful technology has to offer. At present there are three analytical methods available: the newly released Affymetrix **Microarray** Suite 5.0 (AMS) software that accompanies the GeneChip product, the method of Li and Wong (LW; Li and Wong, 2001), and the method of Naef et al. (FN; Naef et al., 2001). The AMS method is tailored for analysis of a single **microarray**, and can therefore be used with any experimental design. The LW method on the other hand depends on a large number of **microarrays** in an experiment and cannot be used for an isolated **microarray**, and the FN method is particular to paired **microarrays**, such as resulting from an experiment in which each 'treatment' sample has a corresponding 'control' sample. Our focus is on analysis of experiments in which there is a series of samples. In this case only the AMS, LW, and the method described in this paper can be used. The present method is model-based, like the LW method, but assumes multiplicative not additive noise, and employs elimination of statistically significant outliers for improved results. Unlike LW and AMS, we do not assume probe-specific background (measured by the so-called mismatch probes). Rather, we assume uniform background, whose level is estimated using both the mismatch and perfect match probe intensities. RESULTS: We present a new method for GeneChip analysis, based on a statistical model with multiplicative noise. We demonstrated that this method yields results superior to those obtained by the Affymetrix **Microarray** Suite 5.0 software and to those obtained by the model-based method of Li and Wong (Li and Wong, 2001). The present method eliminates the hard-to-interpret negative expression indices, and the binary 'presence' calls (present or absent) are replaced by the statistical significance (p-value) of gene expression. We have found that thresholding the p-values at the (0.1)(16)-level produces about the same number of 'present' calls as the AMS software. By testing our method on a pair of replicate GeneChips (hybridized with the same cRNA), we found that 95.6% of data points lie within the 1.25-fold interval. In other words, our method had a 4.4% type I error rate at the 1.25-fold level. The error rate of the LW method was 15%, and that of the AMS method was 29%. There were no points outside the 2-fold interval with the present method. Analysis of variance (ANOVA) of another experiment with multiple replicates shows that this reduction of variance is not accompanied by a corresponding reduction of signal. On the contrary, the **signal** -to-**noise** ratio (as measured by the distribution of F-statistics) of the present method is on average 3.4-times better than that of AMS, and 1.4-times better than that of Li and Wong.

L2 ANSWER 17 OF 37 MEDLINE on STN DUPLICATE 6
AN 2002663499 MEDLINE
DN 22310729 PubMed ID: 12424119
TI Statistical analysis of a small set of time-ordered gene expression data using linear splines.

AU De Hoon M J L; Imoto S; Miyano S
CS Human Genome Center, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo, 108-8639, Japan.. mdehoon@ims.u-tokyo.ac.jp
SO BIOINFORMATICS, (2002 Nov) 18 (11) 1477-85.
Journal code: 9808944. ISSN: 1367-4803.
CY England: United Kingdom
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(VALIDATION STUDIES)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20021109
Last Updated on STN: 20030617
Entered Medline: 20030616
AB MOTIVATION: Recently, the temporal response of genes to changes in their environment has been investigated using cDNA **microarray** technology by measuring the gene expression levels at a small number of time points. Conventional techniques for time series analysis are not suitable for such a short series of time-ordered data. The analysis of gene expression data has therefore usually been limited to a fold-change analysis, instead of a systematic statistical approach. METHODS: We use the **maximum likelihood** method together with Akaike's Information Criterion to fit linear splines to a small set of time-ordered gene expression data in order to infer statistically meaningful information from the measurements. The significance of measured gene expression data is assessed using Student's t-test. RESULTS: Previous gene expression measurements of the cyanobacterium Synechocystis sp. PCC6803 were reanalyzed using linear splines. The temporal response was identified of many genes that had been missed by a fold-change analysis. Based on our statistical analysis, we found that about four gene expression measurements or more are needed at each time point.

L2 ANSWER 18 OF 37 MEDLINE on STN DUPLICATE 7
AN 2002494063 MEDLINE
DN 22205932 PubMed ID: 12217912
TI Ratio statistics of gene expression levels and applications to **microarray** data analysis.
AU Chen Yidong; Kamat Vishnu; Dougherty Edward R; Bittner Michael L; Meltzer Paul S; Trent Jeffery M
CS Cancer Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Building 50, Room 5154, 50 South Drive, MSC 8000, Bethesda, MD 20892, USA.
SO BIOINFORMATICS, (2002 Sep) 18 (9) 1207-15.
Journal code: 9808944. ISSN: 1367-4803.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021002
Last Updated on STN: 20021213
Entered Medline: 20021106
AB MOTIVATION: Expression-based analysis for large families of genes has recently become possible owing to the development of cDNA **microarrays**, which allow simultaneous measurement of transcript levels for thousands of genes. For each spot on a **microarray**, signals in two channels must be extracted from their backgrounds. This requires algorithms to extract signals arising from tagged mRNA hybridized to arrayed cDNA locations and algorithms to determine the significance of signal ratios. RESULTS: This paper focuses on estimation of signal ratios from the two channels, and the significance of those ratios. The key issue is the determination of whether a ratio is significantly high or low

in order to conclude whether the gene is upregulated or downregulated. The paper builds on an earlier study that involved a hypothesis test based on a ratio statistic under the supposition that the measured fluorescent intensities subsequent to image processing can be assumed to reflect the signal intensities. Here, a refined hypothesis test is considered in which the measured intensities forming the ratio are assumed to be combinations of signal and background. The new method involves a **signal**-to-**noise** ratio, and for a high **signal**-to-**noise** ratio the new test reduces (with close approximation) to the original test. The effect of low **signal**-to-**noise** ratio on the ratio statistics constitutes the main theme of the paper. Finally, and in this vein, a quality metric is formulated for spots. This measure can be used to decide whether or not a spot ratio should be deleted, or to adjust various measurements to reflect confidence in the quality of the measurement. CONTACT: e-dougherty@tamu.edu

L2 ANSWER 19 OF 37 MEDLINE on STN
AN 2002661834 MEDLINE
DN 22309070 PubMed ID: 12421134
TI Robustness of the Chen-Dougherty-Bittner procedure against non-normality and heterogeneity in the coefficient of variation.
AU Powell Douglas A; Anderson Lucy M; Cheng Robert Y S; Alvord W Gregory
CS National Cancer Institute at Frederick, Data Management Services, Frederick, Maryland 21702-1201, USA.
SO JOURNAL OF BIOMEDICAL OPTICS, (2002 Oct) 7 (4) 650-60.
Journal code: 9605853. ISSN: 1083-3668.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20021108
Last Updated on STN: 20030502
Entered Medline: 20030501
AB Chen, Dougherty, and Bittner [Y. Chen, E. R. Dougherty, and M. L. Bittner, J. Biomed. Opt. 2(4), 364-374 (1997)] provided the derivation of a probability density function (PDF) for a signal ratio from a DNA **microarray**. This PDF is potentially useful for testing whether a pair of signals from the same gene has a common mean. The derivation of the PDF assumes the normality of all signal distributions and a common coefficient of variation (CV) for all signals within a **microarray**. The testing procedure requires the calculation of a common confidence interval for a **microarray**, based on a **maximum likelihood** estimator of the "common" CV, and the determination of whether or not a ratio for a particular gene falls within this interval. This study used Monte Carlo techniques and demonstrated that the procedure is robust to violations of normality and also to constancy in the coefficients of variation. A closer examination of the dynamics of the procedure found that the robustness was the result of offsetting effects. The size of the confidence interval was increased as a result of higher estimates of the common CV, as the actual CV pattern became heterogeneous. This effect mitigated the inflation in the size of the ratio as a result of increasing CV heterogeneity. These findings suggest that the Chen-Dougherty-Bittner procedure may be used even if underlying assumptions do not hold.

L2 ANSWER 20 OF 37 MEDLINE on STN DUPLICATE 8
AN 2003026463 MEDLINE
DN 22313754 PubMed ID: 12425984
TI Zipf's law in importance of genes for cancer classification using **microarray** data.
AU Li Wentian; Yang Yaning
CS Center for Genomics and Human Genetics North Shore LIJ Research Institute, 350 Community Drive, Manhasset, NY 11030, USA.. wli@nlij-genetics.org

NC HG00008 (NHGRI)
K01HG00024 (NHGRI)
N01-AR12256 (NIAMS)
SO JOURNAL OF THEORETICAL BIOLOGY, (2002 Dec 21) 219 (4) 539-51.
Journal code: 0376342. ISSN: 0022-5193.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20030122
Last Updated on STN: 20030206
Entered Medline: 20030205
AB Using a measure of how differentially expressed a gene is in two biochemically/phenotypically different conditions, we can rank all genes in a **microarray** dataset. We have shown that the falling-off of this measure (normalized **maximum likelihood** in a classification model such as logistic regression) as a function of the rank is typically a power-law function. This power-law function in other similar ranked plots are known as the Zipf's law, observed in many natural and social phenomena. The presence of this power-law function prevents an intrinsic cutoff point between the "important" genes and "irrelevant" genes. We have shown that similar power-law functions are also present in permuted dataset, and provide an explanation from the well-known chi(2) distribution of likelihood ratios. We discuss the implication of this Zipf's law on gene selection in a **microarray** data analysis, as well as other characterizations of the ranked likelihood plots such as the rate of fall-off of the likelihood.

=> d 21-37 bib ab

L2 ANSWER 21 OF 37 MEDLINE on STN DUPLICATE 9
AN 2002190518 MEDLINE
DN 21921160 PubMed ID: 11923847
TI Genome-wide detection of chromosomal imbalances in tumors using BAC **microarrays**.
AU Cai Wei-Wen; Mao Jian-Hua; Chow Chi-Wen; Damani Shamsha; Balmain Allan; Bradley Allan
CS Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX 77030, USA.
SO NATURE BIOTECHNOLOGY, (2002 Apr) 20 (4) 393-6.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020403
Last Updated on STN: 20020724
Entered Medline: 20020723
AB Chromosomal imbalances such as deletions and amplifications are common rearrangements in most tumors. Specific rearrangements are consistently associated with specific tumor types or stages, implicating the role of the genes in a region of chromosomal imbalance in tumor initiation and progression. The development of comparative genomic hybridization (CGH) has obviated the need to obtain metaphase spreads from tumors, so that the chromosomal imbalances in many solid tumors may be revealed using an extracted genomic DNA sample. However, the resolution of the cytogenetic method remains and the extreme technical difficulty of CGH has restricted its use. Conceptually, DNA **microarray**-based CGH is an obvious solution to all of the limitations of conventional CGH. Although arrays have been used for CGH studies, their success has been limited by poor specific **signal**-to-**noise** ratios. Here we demonstrate

a **microarray**-based CGH method that allows reliable detection of chromosomal deletions and amplifications with high resolution. Our **microarray** system is fundamentally different from most current **microarray** technologies in that activated DNA is printed on natural glass surfaces while other systems almost exclusively focus on activating the surfaces, a strategy that invariably introduces hybridization backgrounds. The concept of using pre-modification may be generally applied for making arrays of other biological materials, as modifying the substrates will be more controllable in solution than on surfaces.

L2 ANSWER 22 OF 37 MEDLINE on STN
AN 2002415301 IN-PROCESS
DN 22159484 PubMed ID: 12169536
TI Variance stabilization applied to **microarray** data calibration and to the quantification of differential expression.
AU Huber Wolfgang; Von Heydebreck Anja; Sultmann Holger; Poustka Annemarie; Vingron Martin
CS Department of Molecular Genome Analysis, German Cancer Research Center, INF 280, Heidelberg, 69120, Germany Department of Computational Molecular Biology, Max-Planck-Institute for Molecular Genetics, Dahlem, Berlin, 14195, Germany.
SO BIOINFORMATICS, (2002 Jul) 18 Suppl 1 S96-S104.
Journal code: 9808944. ISSN: 1367-4803.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20020810
Last Updated on STN: 20021212
AB We introduce a statistical model for **microarray** gene expression data that comprises data calibration, the quantification of differential expression, and the quantification of measurement error. In particular, we derive a transformation h for intensity measurements, and a difference statistic Deltah whose variance is approximately constant along the whole intensity range. This forms a basis for statistical inference from **microarray** data, and provides a rational data pre-processing strategy for multivariate analyses. For the transformation h, the parametric form h(x)=arsinh(a+bx) is derived from a model of the variance-versus-mean dependence for **microarray** intensity data, using the method of variance stabilizing transformations. For large intensities, h coincides with the logarithmic transformation, and Deltah with the log-ratio. The parameters of h together with those of the calibration between experiments are estimated with a robust variant of **maximum-likelihood** estimation. We demonstrate our approach on data sets from different experimental platforms, including two-colour cDNA arrays and a series of Affymetrix oligonucleotide arrays. Availability: Software is freely available for academic use as an R package at http://www.dkfz.de/abt0840/whuber Contact: w.huber@dkfz.de

L2 ANSWER 23 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:116848 BIOSIS
DN PREV200200116848
TI The bioinformatics of **microarray** gene expression profiling.
AU Weinstein, John N. (1); Scherf, Uwe; Lee, Jae K.; Nishizuka, Satoshi; Gwadry, Fuad; Ajay; Bussey, Kim; Kim, S.; Smith, Lawrence H.; Tanabe, Lorraine; Richman, Samuel; Alexander, Jessie; Kouros-Mehr, Hosein; Maunakea, Alika; Reinhold, William C.
CS (1) National Institutes of Health, 9000 Rockville Pike, Bldg 37, Rm 4E-28, Bethesda, MD, 20892: weinstein@dtpax2.ncifcrf.gov USA
SO Cytometry, (January 1, 2002) Vol. 47, No. 1, pp. 46-49.
http://www.interscience.wiley.com/jpages/0196-4763/. print.
ISSN: 0196-4763.
DT Article

LA English

L2 ANSWER 24 OF 37 MEDLINE on STN
AN 2002195782 MEDLINE
DN 21926473 PubMed ID: 11928474
TI Singular value decomposition regression models for classification of tumors from **microarray** experiments.
AU Ghosh Debashis
CS Department of Biostatistics, University of Michigan, 1420 Washington Heights, Ann Arbor, MI 48109-2029, USA.. ghoshd@umich.edu
SO PACIFIC SYMPOSIUM ON BIOCOMPUTING, (2002) 18-29.
Journal code: 9711271.
CY Singapore
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200210
ED Entered STN: 20020404
Last Updated on STN: 20021002
Entered Medline: 20021001
AB An important problem in the analysis of **microarray** data is correlating the high-dimensional measurements with clinical phenotypes. In this paper, we develop predictive models for associating gene expression data from **microarray** experiments with such outcomes. They are based on the singular value decomposition. We propose new algorithms for performing gene selection and gene clustering based on these predictive models. The estimation procedure using the regression models occurs in two stages. First, the gene expression measurements are transformed using the singular value decomposition. The regression parameters in the model linking the principal components with the clinical responses are then estimated using **maximum likelihood**. We demonstrate the application of the methodology to data from a breast cancer study.

L2 ANSWER 25 OF 37 MEDLINE on STN
AN 2002112317 MEDLINE
DN 21831105 PubMed ID: 11842121
TI Normalization for cDNA **microarray** data: a robust composite method addressing single and multiple slide systematic variation.
AU Yang Yee Hwa; Dudoit Sandrine; Luu Percy; Lin David M; Peng Vivian; Ngai John; Speed Terence P
CS Department of Statistics, Helen Wills Neuroscience Institute, University of California, Berkeley, CA 94720-3860, USA.
NC 5R01MH61665-02 (NIMH)
8R01GM59506A (NIGMS)
SO NUCLEIC ACIDS RESEARCH, (2002 Feb 15) 30 (4) e15.
Journal code: 0411011. ISSN: 1362-4962.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020215
Last Updated on STN: 20020305
Entered Medline: 20020304
AB There are many sources of systematic variation in cDNA **microarray** experiments which affect the measured gene expression levels (e.g. differences in labeling efficiency between the two fluorescent dyes). The term normalization refers to the process of removing such variation. A constant adjustment is often used to force the distribution of the intensity log ratios to have a median of zero for each slide. However, such global normalization approaches are not adequate in situations where dye biases can depend on spot overall intensity and/or spatial location within the array. This article proposes normalization methods that are

based on robust local regression and account for intensity and spatial dependence in dye biases for different types of cDNA **microarray** experiments. The selection of appropriate controls for normalization is discussed and a novel set of controls (**microarray** sample pool, MSP) is introduced to aid in intensity-dependent normalization. Lastly, to allow for comparisons of expression levels across slides, a robust method based on **maximum likelihood** estimation is proposed to adjust for scale differences among slides.

L2 ANSWER 26 OF 37 MEDLINE on STN
AN 2002080735 MEDLINE
DN 21665999 PubMed ID: 11806820
TI Characterization of the expression ratio noise structure in high-density oligonucleotide arrays.
AU Naef Felix; Hacker Coleen R; Patil Nila; Magnasco Marcelo
CS Mathematical Physics laboratory, Center for Studies in Physics and Biology, The Rockefeller University, 1230 York Ave, NY 10021, USA.. felix@funes.rockefeller.edu
SO GENOMEBIOLOGY.COM, (2002) 3 (1) PREPRINT0001.
Journal code: 100960660. ISSN: 1465-6914.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020128
Last Updated on STN: 20030105
Entered Medline: 20020502
AB BACKGROUND: High-density oligonucleotide **microarrays** provide a powerful tool for assessing differential mRNA expression levels. Characterizing the noise resulting from the enzymatic and hybridization steps, called type I noise, is essential for attributing significance measures to the differential expression scores. We introduce scoring functions for expression ratios, and associated quality measures. Both the PM (Perfect Match) probes and PM-MM differentials (MM is the single MisMatch) are considered as raw intensities. We then characterize the log-ratio noise structure using robust estimates of their intensity dependent variance. RESULTS: We show the relationships between the obtained ratios and their quality measures. The complementarity of PM and PM-MM methods is emphasized by the probe sets **signal** to **noise** measures. Using a large set of replicate experiments, we demonstrate that the noise structure in the log-ratios very closely follows a local log-normal distribution for both the PM and PM-MM cases. Therefore, significance relative to the type I noise can be quantified reliably using the local STD. We discuss the intensity dependence of the STD and show that ratio scores >1.25 are significant in the mid- to high-intensity range. CONCLUSIONS: The ratio noise structure inherent to high-density oligonucleotide arrays can be well described in terms of local log-normal ratio distributions with characteristic intensity dependence. Therefore, robust estimates of the local STD of these distributions provide a simple and powerful way for assessing significance (relative to type I noise) in differential gene expression. This approach will be helpful for improving the reliability of predictions from hybridization experiments in general.

L2 ANSWER 27 OF 37 MEDLINE on STN DUPLICATE 10
AN 2001530381 MEDLINE
DN 21460770 PubMed ID: 11577126
TI High quality RNA isolation from tumours with low cellularity and high extracellular matrix component for cDNA **microarrays**: application to chondrosarcoma.
AU Baelde H J; Cleton-Jansen A M; van Beerendonk H; Namba M; Bovee J V; Hogendoorn P C
CS Department of Pathology, Leiden University Medical Centre, PO Box 9600,

L1-Q, 2300 RC Leiden, The Netherlands.
SO JOURNAL OF CLINICAL PATHOLOGY, (2001 Oct) 54 (10) 778-82.
Journal code: 0376601. ISSN: 0021-9746.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200112
ED Entered STN: 20011001
Last Updated on STN: 20020122
Entered Medline: 20011204
AB AIMS: High quality RNA isolation from cartilaginous tissue is considered difficult because of relatively low cellularity and the abundance of extracellular matrix rich in glycosaminoglycans and collagens. Given the growing interest and technical possibilities to study RNA expression at a high throughput level, research on tissue with these characteristics is hampered by the lack of an efficient method for obtaining sufficient amounts of high quality RNA. METHODS: This paper presents a robust protocol combining two RNA isolation procedures, based on a combination of Trizol and RNA specific columns, which has been developed to obtain high molecular weight RNA from fresh frozen and stored tissue of normal cartilage and cartilaginous tumours. Using this method, RNA was isolated from normal cartilage, peripheral chondrosarcoma, and central chondrosarcoma. RESULTS: The yields ranged from 0.1 to 0.5 microg RNA/mg tissue. RNA isolated with this method was stable and of high molecular weight. RNA samples from normal cartilage and from two chondrosarcomas isolated using this method were applied successfully in cDNA **microarray** experiments. The number of genes that give interpretable results was in the range of what would be expected from **microarray** results obtained on chondrosarcoma cell line RNA. **Signal** to **noise** ratios were good and differential expression between tumour and normal cartilage was detectable for a large number of genes. CONCLUSION: With this newly developed isolation method, high quality RNA can be obtained from low cellular tissue with a high extracellular matrix component. These procedures can also be applied to other tumour material.

L2 ANSWER 28 OF 37 MEDLINE on STN DUPLICATE 11
AN 2001700078 MEDLINE
DN 21615120 PubMed ID: 11747614
TI Bayesian estimation of fold-changes in the analysis of gene expression: the PFOLD algorithm.
AU Theilhaber J; Bushnell S; Jackson A; Fuchs R
CS Aventis Pharmaceuticals, Cambridge Genomics Center, 26 Landsdowne Street, Cambridge, MA 02139, USA.. joachimtheilhaber@aventis.com
SO JOURNAL OF COMPUTATIONAL BIOLOGY, (2001) 8 (6) 585-614.
Journal code: 9433358. ISSN: 1066-5277.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20011219
Last Updated on STN: 20020305
Entered Medline: 20020304
AB A general and detailed noise model for the DNA **microarray** measurement of gene expression is presented and used to derive a Bayesian estimation scheme for expression ratios, implemented in a program called PFOLD, which provides not only an estimate of the fold-change in gene expression, but also confidence limits for the change and a P-value quantifying the significance of the change. Although the focus is on oligonucleotide **microarray** technologies, the scheme can also be applied to cDNA based technologies if parameters for the noise model are provided. The model unifies estimation for all signals in that it

provides a seamless transition from very low to very high **signal**-to-**noise** ratios, an essential feature for current **microarray** technologies for which the median **signal**-to-**noise** ratios are always moderate. The dual use, as decision statistics in a two-dimensional space, of the P-value and the fold-change is shown to be effective in the ubiquitous problem of detecting changing genes against a background of unchanging genes, leading to markedly higher sensitivities, at equal selectivity, than detection and selection based on the fold-change alone, a current practice until now.

L2 ANSWER 29 OF 37 MEDLINE on STN
AN 2003378484 MEDLINE
DN 22795517 PubMed ID: 12914081
TI Nanofilms and nanoclusters: energy sources driving fluorophores of biochip bound labels.
AU Stich N; Gandhum A; Matushin V; Mayer C; Bauer G; Schalkhammer T
CS Kluyver Laboratorium for Biotechnology, TU Delft, Julianalaan 67, 2628 BC Delft, The Netherlands.
SO J Nanosci Nanotechnol, (2001 Dec) 1 (4) 397-405.
Journal code: 101088195. ISSN: 1533-4880.
CY United States
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200309
ED Entered STN: 20030814
Last Updated on STN: 20030917
Entered Medline: 20030916
AB Nanoclusters and nanofilms have the potential to amplify fluorescence and thus to enhance the signal of labeled biomolecules on biochip surfaces. Fluorescent molecules are bound at a certain distance to a resonant layer of a metal or a semiconductor or both, resulting in enhanced absorption and emission of the fluorophore within the electromagnetic near-field. This property makes the system highly useful for interaction studies, including those of DNA and proteins. Due to the amount of data, derived from various sequencing projects and from Proteomic interaction studies within the next years, **microarrays** (or biochips) will represent a central technology in every lab facilitating high-throughput screening and being easily interfaced with computer databases. However, most chips suffer from the disadvantage of insufficient **signal**-to-**noise** (background) ratio and are thus limited to molecules of medium-to-high abundance. Novel approaches are needed for identification of, e.g., low copy RNAs or regulatory proteins. Here we present a study, using novel surface enhanced chips in the standard glass-slide-formats. Applying surface-enhanced fluorescence (SEF), the chips turned out to be useful for interaction studies, such as DNA hybridization, thereby strongly enhancing the on-chip-signals. Compared to standard glass-slide-DNA chips, both the fluorescent signals as well as **signal**-to-**noise** ratio were considerably higher.

L2 ANSWER 30 OF 37 MEDLINE on STN DUPLICATE 12
AN 2001177068 MEDLINE
DN 21039019 PubMed ID: 11196312
TI Maximization of signal derived from cDNA **microarrays**.
AU Wildsmith S E; Archer G E; Winkley A J; Lane P W; Bugelski P J
CS SmithKline Beecham Pharmaceuticals, Hertfordshire, UK..
sophie_e_wildsmith@sbphrd.com
SO BIOTECHNIQUES, (2001 Jan) 30 (1) 202-6, 208.
Journal code: 8306785. ISSN: 0736-6205.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329
AB **Microarray** technology is a powerful tool for generating expression data on a large number of genes simultaneously. However, as for any assay, it must be reproducible to give confidence in the results. Using a classical statistical method--the factorial design of experiments--we have assessed the effects of different experimental factors in our system. Significant effects on signal were seen when the standard components were substituted with a different enzyme, fluorescent label, or RNA purification method. This has led to the implementation of an improved procedure that maximizes signal without affecting the variability of the system, thus increasing the **signal**-to-**noise** ratio. In addition, we were able to quantify the variability between **microarrays** and replicates within **microarrays**.

L2 ANSWER 31 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:245333 BIOSIS
DN PREV200100245333
TI Method and apparatus for analyzing hybridized biochip patterns using resonance interactions employing quantum expressor functions.
AU Gulati, Sandeep (1)
CS (1) La Canada, CA USA
ASSIGNEE: ViaLogy Corporation, Altadena, CA, USA
PI US 6136541 October 24, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 24, 2000) Vol. 1239, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB A technique is described for identifying mutations, if any, present in a biological sample, from a pre-selected set of known mutations. The method can be applied to DNA, RNA and peptide nucleic acid (PNA) **microarrays**. The method analyzes a dot spectrogram representative of quantized hybridization activity of oligonucleotides in the sample to identify the mutations. In accordance with the method, a resonance pattern is generated which is representative of nonlinear resonances between a stimulus pattern associated with the set of known mutations and the dot spectrogram. The resonance pattern is interpreted to a yield a set of confirmed mutations by comparing resonances found therein with predetermined resonances expected for the selected set of mutations. In a particular example, the resonance pattern is generated by iteratively processing the dot spectrogram by performing a convergent reverberation to yield a resonance pattern representative of resonances between a predetermined set of selected Quantum Expressor Functions and the dot spectrogram until a predetermined degree of convergence is achieved between the resonances found in the resonance pattern and resonances expected for the set of mutations. The resonance pattern is analyzed to a yield a set of confirmed mutations by mapping the confirmed mutations to known diseases associated with the pre-selected set of known mutations to identify diseases, if any, indicated by the biological sample. By exploiting a resonant interaction, mutation signatures may be robustly identified even in circumstances involving low **signal** to **noise** ratios or, in some cases, negative **signal** to **noise** ratios.

L2 ANSWER 32 OF 37 MEDLINE on STN
AN 2001091682 MEDLINE
DN 21021028 PubMed ID: 11140756
TI High-resolution near-infrared imaging of DNA **microarrays** with time-resolved acquisition of fluorescence lifetimes.
AU Waddell E; Wang Y; Stryjewski W; McWhorter S; Henry A C; Evans D; McCarley

R L; Soper S A
CS Louisiana State University, Department of Chemistry, Baton Rouge 70803-1804, USA.
NC R01-01499 (NCI)
R23-CA84625
SO ANALYTICAL CHEMISTRY, (2000 Dec 15) 72 (24) 5907-17.
Journal code: 0370536. ISSN: 0003-2700.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010125
AB Ultrasensitive, near-infrared (NIR), time-resolved fluorescence is evaluated as a detection method for reading DNA hybridization events on solid surfaces for **microarray** applications. In addition, the potential of mulitiplexed analyses using time-resolved identification protocols is described. To carry out this work, a NIR time-resolved confocal imager was constructed to read fluorescence signatures from the arrays. The device utilized a 780-nm pulsed diode laser, a single-photon avalanche diode (SPAD), and a high-numerical-aperture microscope objective mounted in an epi-illumination format. Due to the small size of the components that are required to construct this imager, the entire detector could easily be mounted on high-resolution translational stages and scanned over the stationary arrays. The instrument response function of the device was determined to be 275 ps (fwhm), which is adequate for measuring fluorophores with subnanosecond lifetimes. To characterize the system, NIR dyes were deposited directly on different substrate materials typically used for DNA **microarrays**, and the fluorescence lifetimes of two representative dyes were measured. The fluorescence lifetime for aluminum tetrasulfonated naphthalocyanine was found to be 1.92 ns, and a value of 1.21 ns was determined for the tricarbocyanine dye, IRD800, when it was deposited onto poly(methyl methacrylate) (PMMA) and measured in the dry state. Finally, the imager was used to monitor hybridization events using probe oligonucleotides chemically tethered to a PMMA substrate via a glutardialdehyde linkage to an aminated-PMMA surface. The limit of detection for oligonucleotides containing a NIR fluorescent reporter was determined to be 0.38 molecules/microm2, with this detection limit improving by a factor of 10 when a time-gate was implemented. Fluorescence lifetime analysis of the hybridization events on PMMA indicated a lifetime value of 1.23 ns for the NIR-labeled oligonucleotides when using **maximum-likelihood** estimators.

L2 ANSWER 33 OF 37 MEDLINE on STN DUPLICATE 13
AN 2001293351 MEDLINE
DN 21276497 PubMed ID: 11382363
TI Testing for differentially-expressed genes by **maximum-likelihood** analysis of **microarray** data.
AU Ideker T; Thorsson V; Siegel A F; Hood L E
CS Department of Molecular Biotechnology, University of Washington, Seattle, WA 98195, USA.. tideker@systemsbiology.org
SO JOURNAL OF COMPUTATIONAL BIOLOGY, (2000) 7 (6) 805-17.
Journal code: 9433358. ISSN: 1066-5277.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719
AB Although two-color fluorescent DNA **microarrays** are now standard

equipment in many molecular biology laboratories, methods for identifying differentially expressed genes in **microarray** data are still evolving. Here, we report a refined test for differentially expressed genes which does not rely on gene expression ratios but directly compares a series of repeated measurements of the two dye intensities for each gene. This test uses a statistical model to describe multiplicative and additive errors influencing an array experiment, where model parameters are estimated from observed intensities for all genes using the method of **maximum likelihood**. A generalized likelihood ratio test is performed for each gene to determine whether, under the model, these intensities are significantly different. We use this method to identify significant differences in gene expression among yeast cells growing in galactose-stimulating versus non-stimulating conditions and compare our results with current approaches for identifying differentially-expressed genes. The effect of sample size on parameter optimization is also explored, as is the use of the error model to compare the within- and between-slide intensity variation intrinsic to an array experiment.

L2 ANSWER 34 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:183420 BIOSIS
DN PREV200200183420
TI A novel, sensitive detection system for high-density **microarrays** using dendrimer technology.
AU Stears, Robin L.; Getts, Robert C.; Gullans, Steven R. (1)
CS (1) Brigham and Women's Hospital, Dept. of Medicine, Renal Division, Harvard Institutes of Medicine, 77 Ave. Louis Pasteur, Boston, MA, 02115: sgullans@rics.bwh.harvard.edu USA
SO Physiological Genomics, (September, 2000) Vol. 3, pp. 93-99. http://www.physiolgenomics.org. print. ISSN: 1094-8341.
DT Article
LA English
AB To improve signal detection on cDNA **microarrays**, we adapted a fluorescent oligonucleotide dendrimeric signal amplification system to **microarray** technology. This signal detection method requires 16-fold less RNA for probe synthesis, does not depend on the incorporation of fluorescent dNTPs into a reverse transcription reaction, generates a high signal-to-background ratio, and can be used to allow for multichannel detection on a single chip. Furthermore, since the dendrimers can be detected individually, it may be possible, by employing dendrimer-binding standards, to calculate the numbers of bound cDNAs can be estimated. These features make the dendrimer signal detection reagent ideal for high-throughput functional genomics research.

L2 ANSWER 35 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:111279 BIOSIS
DN PREV199698683414
TI Determination of acetylcholine and choline with platinum-black ultramicroarray electrodes using liquid chromatography with a post-column enzyme reactor.
AU Niwa, Osamu (1); Horiuchi, Tsutomu; Morita, Masao; Huang, Tiehua; Kissinger, Peter T.
CS (1) NTT Basic Res. Lab., Nippon Telegraph Telephone Corp., 3-1 Morinosato, Wakamiya, Atsugi, Kanagawa 243-01 Japan
SO Analytica Chimica Acta, (1996) Vol. 318, No. 2, pp. 167-173. ISSN: 0003-2670.
DT Article
LA English
AB A method for the highly sensitive determination of acetylcholine (ACh) and choline (Ch) was developed using platinum (Pt) black **microarray** electrodes as detectors in a microbore liquid chromatography (LC) with a post column enzyme reactor. The electrodes were prepared by plating a gold (Au) film electrode with sub-mu-m Pt-black particles. Since hydrogen peroxide generated by the enzymatic reaction of ACh and Ch was oxidized

only at the Pt-black **microarray** electrode, each Pt-black particle (typically 0.1-0.2 mu-m in size) operated as an ultramicroelectrode. A high **signal**-to-**noise** ratio was achieved because of the high current density at the Pt-black **microarray** electrodes and because the Au film has a much lower baseline noise than the Pt. Detection limits of 5.7 (ACh) and 6.0 (Ch) fmol were obtained, with a wide linear range. The ACh and Ch signals with an Au film electrode modified with Pt-black particles retained more than 70% of their initial value after 5 days with continuous potential application. This is better stability than for a bare platinum electrode which retained only 40% of its initial response under comparable conditions.

L2 ANSWER 36 OF 37 MEDLINE on STN DUPLICATE 14
AN 95236649 MEDLINE
DN 95236649 PubMed ID: 7720246
TI Electrochemical determination of low blood lead concentrations with a disposable carbon **microarray** electrode.
AU Feldman B J; D'Alessandro A; Osterloh J D; Hata B H
CS University of California/San Francisco, UCSF/SFGH Metals Laboratory, San Francisco General Hospital 94110, USA.
NC R08/CCR908611 (NIEHS)
R55/ES05791
SO CLINICAL CHEMISTRY, (1995 Apr) 41 (4) 557-63.
Journal code: 9421549. ISSN: 0009-9147.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
ED Entered STN: 19950605
Last Updated on STN: 19970203
Entered Medline: 19950522
AB Lead concentrations in blood samples typical of unexposed individuals are determined by using square-wave anodic stripping voltammetry at a disposable 287-element (15-35-microns diameter) carbon **microarray** electrode. Analysis of a series of low Pb-containing samples (blood [Pb] = 17 to 92 micrograms/L) by standard addition gives good accuracy (average bias vs graphite furnace atomic absorption spectroscopy = -4 micrograms/L) and precision (pooled SD = 7 micrograms/L). The **signal**/**noise** ratio is improved by about an order of magnitude over that found at a single carbon disk (10 microns diameter), resulting in a detection limit (for the **microarray**) of 5 micrograms/L for a 60-s deposition of sample.

L2 ANSWER 37 OF 37 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1985:374634 BIOSIS
DN BA80:44626
TI **MICROARRAY** ELECTROCHEMICAL FLOW DETECTORS AT HIGH APPLIED POTENTIALS AND LIQUID CHROMATOGRAPHY WITH ELECTROCHEMICAL DETECTION OF CARBAMATE PESTICIDES IN RIVER WATER.
AU ANDERSON J L; WHITEN K K; BREWSTER J D; OU T-Y; NONIDEZ W K
CS DEP. CHEM., UNIV. GA., ATHENS, GA. 30602.
SO ANAL CHEM, (1985) 57 (7), 1366-1373.
CODEN: ANCHAM. ISSN: 0003-2700.
FS BA; OLD
LA English
AB The properties and advantages of **microarray** electrodes were discussed relative to solid electrodes as flow detectors. Amperometric response for a series of Kelgraf **microarray** electrodes of varying percent graphite was in agreement with theoretical predictions. The Kelgraf electrode effectively discriminates between oxidation reactions limited by the rate of mass transport and reactions (including solvent oxidation) limited by the rate of electron transfer or other

surface processes, affording improved detection limits at high applied potentials. The advantages were illustrated for measurement of carbamate pesticides spiked into a river water matrix, using liquid chromatography [LC] with electrochemical detection. Subnanogram detection limits (in the 50-430-pg range) were obtained in all cases with minimal sample cleanup or pretreatment, with as much as 60-fold improvement over other reports for glassy carbon or alternative LC detectors in the best cases. The relative magnitudes of pesticide current response at Kelgraf and glassy carbon electrodes under identical conditions were consistent with theoretical predictions, while enhancements in the **signal/noise** ratio were slightly lower than expected. [Aminocarb, Carbendazim, Desmedipham and Dichloran were studied.]

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---Logging off of STN---

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.69	35.90

STN INTERNATIONAL LOGOFF AT 16:47:36 ON 26 SEP 2003